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09/731,366	12/06/2000	Joshua S. Salafsky	0575/60934/JPW/ADM	8346

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Cooper & Dunham LLP
1185 Avenue of the Americas
New York, NY 10036

EXAMINER

COUNTS, GARY W

ART UNIT PAPER NUMBER

1641

DATE MAILED: 09/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

3M.

Office Action Summary

Application No.

09/731,366

Applicant(s)

SALAFSKY ET AL.

Examiner

Gary W. Counts

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 25 June 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-28 and 33-38 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-28 and 33-38 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

Status of the claims

The amendment filed June 25, 2004 is acknowledged and has been entered.

Rejections Withdrawn

The provisional double patenting rejection of claims 1-28 and 33-38 has been withdrawn in light of the abandonment of Application No. 09/907,035.

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

2. Claims 1-4, 6, 12, 13, 21-23, 33, 34 and 36-38 are rejected under 35

U.S.C. 102(e) as being anticipated by Schultz et al (US 6,180,415).

Schultz et al disclose a method for detecting the presence, information about, a target having a molecular feature of interest (col 5 and 6, col 34, line 6 – col 35 line 33). Schultz et al disclose contacting the target with one or more PRE's (labels) having surface localized molecules to produce an interaction between the molecular feature and the localized molecules. Schultz et al disclose that the target contains a ligand-binding site, and the surface localized molecule is a ligand capable of forming a ligand/ligand-binding complex (col 5, lines 60-67). Schultz et al disclose that the PRE's

can accept pulses between 5 to 500 femotsecond for driving second harmonic generation processes. Schultz et al disclose contacting a surface with these PRE's thereby creating an interface at the surface which has target attached thereto wherein the target is not labeled with a non-linear label wherein the target is not detectable at the interface using a surface selective technique and wherein the target is labeled when the PRE comprising the ligand partner for the target attaches to the target and measuring a change in nonlinear optical light at the interface in the presence of the labeled target using a nonlinear optical technique. Schultz et al disclose that the PRE's can be used for cell sorting. Schultz et al disclose analyzing a cell type expressing a particular surface antigen using a particular PRE probe (col 49, lines 55-67).

With respect to second harmonic active-label as recited in the instant claims. In the specification on page 2, lines 19-23 the applicant defines that second harmonic active-labels are second harmonic-active moieties which can be attached to a molecule of interest that is not second harmonic active and applicant further defines (page 8, lines 6-11) that a second harmonic refers to a frequency of light that is twice the frequency of a fundamental beam of light and that a second harmonic-active moiety is a substance which when irradiated with a fundamental beam of light generates a second harmonic of the fundamental. Schultz et al disclose that the PRE's (labels) can accept pulses between 5 to 500 femtosecond for driving second harmonic generation. Therefore, Schultz et al disclose second harmonic labels and thus Schultz et al disclose the same label as recited in the claims and therefore the label of Schultz would be hyperpolarizable and contribute to a net orientation at the interface.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

4. Claims 2, 7, 8, 27 and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schultz et al in view of Quinn et al.

See above for teachings of Schultz et al.

Schultz et al differ from the instant invention in failing to specifically state that the surface selective technique is second harmonic generation.

Quinn et al disclose second harmonic generation and sum-frequency generation techniques utilized with second harmonic labels for detecting molecules of interest.

Although Schultz et al does not specifically state that the use of second harmonic generation as the surface selective technique it would have been obvious to one of ordinary skill in the art to use a surface selective technique such as taught by Quinn et al with the second harmonic label of Schultz et al because Schultz et al specifically teach that their labels can be used in second harmonic generation processes (col 13, lines 57-60).

5. Claims 5, 24 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schultz et al in view of Mattingly et al (US 5,145,790).

See above for teachings of Schultz et al.

Schultz et al differ from the instant invention in failing to disclose the molecule being a pollutant.

Mattingly et al discloses specific binding reagents, such as antibodies, for detecting the presence or amount of polychlorinated biphenyls in a test sample (col 2, lines 10-34).

It would have been obvious to one of ordinary skill in the art to use the polychlorinated biphenyl specific antibodies taught by Mattingly et al in the method of Schultz et al because Schultz et al is generic with respect to the analyte that is to be detected and one would use the appropriate reagent, i.e. antibody to detect the desired analyte, in this case polychlorinated biphenyls.

6. Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Schultz et al in view of Buechler et al (US 6,194,222).

See above for teachings of Schultz et al.

Schultz et al differ from the instant invention in failing to disclose the non-specific interaction being an electrostatic interaction.

Buechler et al disclose labels which are bound to the molecule by electrostatic interactions (col 21, lines 1-10). These interactions allow for an immunoassay system that is simple, rapid and reliable. Reliability in an immunoassay system is critical for the accurate measurement of the analyte (col 1, lines 40-43).

It would have been obvious to one of ordinary skill in the art to incorporate electrostatic interactions as taught by Buechler et al for the binding of the second harmonic-active moiety to the molecule of Schultz et al because Buechler et al shows

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that these interactions allow for an immunoassay system that is simple, rapid and reliable.

7. Claims 10, 11 and 35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schultz et al in view of Wang et al (US 5,696,157).

See above for teachings of Schultz et al.

Schultz et al differ from the instant invention in failing to disclose that the second harmonic-active label is specific for an amine group.

Wang et al disclose labels, which are specific for amine groups. These amine-reactive dyes are of particular relevance as they are commonly used to label proteins and polypeptides (col 13, lines 50-63). These labels are able to preferentially label a specific ingredient or component in a sample and enable the researcher to determine the presence, quantity or location of that specific ingredient or component (col 1, lines 11-19).

It would have been obvious to one of ordinary skill in the art to substitute the label as taught by Wang et al for the label of Schultz et al because Wang et al shows that these amine labels are of particular relevance as they are commonly used to label proteins and polypeptide and that these labels are able to preferentially label a specific ingredient or component in a sample and enable the researcher to determine the presence, quantity or location of that specific ingredient or component.

Furthermore, since the amine-specific dyes of Wang et al is within the chemical class as disclosed in the specification on page 16, line 24 (amine-specific dyes), it is

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considered that the amine-specific dye of Wang et al would be a second-harmonic active moiety.

With respect to the plurality of individual second harmonic-active labels bound together in a fixed and determinate orientation with respect to each other so as to increase the overall nonlinear susceptibility of the second harmonic-active moiety as recited in the instant claims, the optimum overall nonlinear susceptibility of the second harmonic-active moiety can be determined by routine experimentation and thus would have been obvious to one of ordinary skill in the art. Further, it has long been settled to be no more than routine experimentation for one of ordinary skill in the art to discover an optimum value of a result effective variable.

“[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum of workable ranges by routine experimentation.” Application of Aller, 220 F.2d 454,456, 105 USPQ 233, 235-236 (C.C.P.A. 1955). “No invention is involved in discovering optimum ranges of a process by routine experimentation .” Id. At 458,105 USPQ at 236-237. The “discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art.” Application of Boesch, 617 F.2d 272,276, 205 USPQ 215, 218-219 (C.C.P.A. 1980).

8. Claims 14 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schultz et al in view of Eisenthal et al (Photophysics of liquid interfaces by Second Harmonic Spectroscopy, J.Phys. Chem 1996, 100, Vol. 31, 12997-13006).

See above for teachings of Schultz et al.

Schultz et al differ from the instant invention in failing to disclose an air-water interface and a water-glass interface.

Eisenthal et al disclose the investigation of interface properties using second-harmonic spectroscopy. Eisenthal et al disclose studies of molecules at the silica/water interface and at the air/water interface. The study of molecules at these interfaces provides new information and insights into equilibrium and dynamic processes occurring at interfaces. These liquid interfaces not only are of great scientific interest but also directly impact many areas of medicine and technology (page 12998)

It would have been obvious to one of ordinary skill in the art to incorporate the interfaces as taught by Eisenthal et al into the method of Schultz et al because Eisenthal et al show that the study of molecules at these interfaces provide new information and insights into equilibrium and dynamic processes occurring at interfaces and that these liquid interfaces not only are of great scientific interest but also directly impact many areas of medicine and technology.

9. Claim 15 is rejected under 35 U.S.C. 103(a) as being unpatentable over Schultz et al in view of Conboy et al (J. Chem. 1994, 98, 9688-9692).

See above for teachings of Schultz et al.

Schultz et al differ from the instant invention in failing to disclose and oil-water interface.

Conboy et al disclose the investigation of oil-water interfaces. The study of this interface demonstrates the utility of using second harmonic generation to measure properties of the oil-water interface in the absence of any optical resonance's and expand the range of systems, which can be examined, by second harmonic generation (abstract and introduction). Conboy et al also disclose that there is a high interest in the

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characterization of oil-water interfaces because of the central role, which they play in many areas of chemistry, physics, and biology.

It would have been obvious to one of ordinary skill in the art to incorporate the oil-water interface as taught by Conboy et al into the method of Schultz et al because Conboy et al shows that the study of this interface demonstrates the utility of using second harmonic generation to measure properties of oil-water interface in the absence of any optical resonances and expand the range of systems which can be examined by second harmonic generation. Conboy et al also that there is a high interest in the characterization of oil-water interfaces because of the central role, which they play in many areas of chemistry, physics, and biology.

10. Claims 17-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schultz et al in view of Eisenthal et al (US 6,055,051).

See above for teachings of Schultz et al.

Schultz et al differ from the instant invention in failing to specifically state the interface is a cell surface.

Eisenthal et al disclose second harmonic generation and sum frequency generation used for surface analysis. Eisenthal et al disclose that the surface to be investigated can be a biological cell where the substance of interest at the surface of the cell (e.g. cell membrane) is detected. Eisenthal et al shows that the use of such a surface provide for an analytical tool for ascertaining whether or not the substance will adhere to cells, liposomes, emulsions and similar structures (col 4, line 57- col 5, line 5).

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It would have been obvious to one of ordinary skill in the art to incorporate services such as taught by Eienthal et al into the method of Schultz et al because Eienthal et al shows that the use of such a surface provide for an analytical tool for ascertaining whether or not the substance will adhere to cells, liposomes, emulsions and similar structures.

11. Claim 26 is rejected under 35 U.S.C. 103(a) as being unpatentable over Schultz et al in view of Tadano et al (US 5,962,248).

See above for teachings of Schultz et al.

Schultz et al differ from the instant invention in failing to disclose the molecule being a chloride ion.

Tadano et al disclose a reagent for detecting chloride ions in a sample (col 1, line 66 – col 2, line 10).

It would have been obvious to one of ordinary skill in the art to use the enzyme substrate specific for chloride ions taught by Tadano et al in the method of Schultz et al because Schultz is generic with respect to the analyte that is to be detected and one would use the appropriate reagent, i.e. enzyme substrate to detect the desired analyte in this case chloride ion.

Response to Arguments

12. No claims are allowed.

13. Applicant's arguments filed June 25, 2004 have been fully considered but they are not persuasive.

Applicant argues that Schultz et al does not teach or suggest using a surface selective technique, i.e. a technique requiring the labels to have "hyperpolarizability and a net orientation at the interface. Applicant asserts that the PREs of Schultz et al. "can accept" light pulses that can also be used to drive second harmonic-active labels, the PRE's scatter the light at the same wavelength as the light shone on them. This is not found persuasive because this is a statement without support or evidence that Schultz et al does not disclose the second harmonic label. Further, applicant states that Applicants' second harmonic-active labels scatter the light at one-half the wavelength shone on them. This is not found persuasive because applicant hasn't provided support or evidence to show that the label of Applicant is any different than that of Schultz et al nor do the claims positively recite that Applicants' second harmonic-active labels scatter the light at one-half the wavelength shone on them.

Applicant further state that Schultz et al. and related articles, e.g. Schultz et al., "Single-target Molecule Detection with Nonbleaching Multicolor Optical Immunolabels," PNAS, February 1, 2000, vol. 97, No. 3, pp. 996-1001, attached as Exhibit A, that PRE's do not generate a second harmonic. This is not found persuasive because this is a statement without support. Applicant has not directly pointed out in the Schultz et al patent or the Schultz et al article of any difference between the labels and the labels of the instantly recited claims. Further, as stated above and as stated in the previous office action In the specification on page 2, lines 19-23 the applicant defines that second harmonic active-labels are second harmonic-active moieties which can be attached to a molecule of interest that is not second harmonic active and applicant

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further defines (page 8, lines 6-11) that a second harmonic refers to a frequency of light that is twice the frequency of a fundamental beam of light and that a second harmonic-active moiety is a substance which when irradiated with a fundamental beam of light generates a second harmonic of the fundamental. Schultz et al disclose that the PRE's (labels) can accept pulses between 5 to 500 femtosecond for driving second harmonic generation. Therefore, Schultz et al disclose second harmonic labels and since applicant hasn't distinguished the instantly recited labels from that of Schultz et al., it is the Examiner's position that Schultz et al disclose the same label as recited in the claims and therefore the label of Schultz would be hyperpolarizable and contribute to a net orientation at the interface.

Applicant further argues that Schultz et al does not describe the absolute requirement of non-centrosymmetry for second harmonic generation or any intention to use the PREs for second harmonic generation in an assay. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., non-centrosymmetry for second harmonic generation) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Applicant argues that the secondary references do not remedy the deficiencies of Schultz et al. This is not found persuasive because as stated above, it is the Examiner's position that Schultz reads on the instantly recited claims and therefore the

combination of Schultz et al and the secondary references is considered appropriate and read on the instantly recited claims.

Conclusion

14. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary W. Counts whose telephone number is (571) 2720817. The examiner can normally be reached on M-F 8:00 - 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Gary Counts
Examiner
Art Unit 1641
September 3, 2004



LONG V. LE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

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